

Lethal tetanus infection following cytotoxic chemotherapy for advanced breast cancer

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Summary. Tetanus is rarely seen in developed countries where there is therefore less awareness in clinical practice. Necrotic breast tumors may provide a portal of entry for serious tetanus infection. We report on a patient who acquired devastating tetanus infection from necrotic tumor following cytotoxic chemotherapy; we also review similar cases in the literature. Clinical awareness, timely treatment, and proper tetanus vaccination before surgical excision, debridement, or cytotoxic chemotherapy might be necessary to prevent this catastrophe.

Key words: tetanus, breast cancer, complete remission of pathology, immunization

«INFEZIONE LETALE DA TETANO A SEGUITO DI CHEMIOTERAPIA CITOTOSSICA PER CANCRO MAMMARIO AVANZATO»

Riassunto. Il tetano è osservato raramente nei paesi sviluppati dove c'è tuttavia una minor consapevolezza nella pratica clinica. I tumori mammari necrotici possono costituire una via d'accesso per una seria infezione da tetano. Presentiamo il caso di un paziente che ha contratto una devastante infezione da tetano conseguente a chemioterapia citotossica per tumore necrotico; abbiamo inoltre revisionato casi simili in letteratura. La consapevolezza clinica, il trattamento tempestivo, ed una corretta vaccinazione contro il tetano prima di escissione chirurgica, drenaggio o chemioterapia citotossica potrebbero essere necessari per prevenire tale catastrofe.

Parole chiave: tetano, cancro mammario, remissione completa della patologia, immunizzazione

Introduction

Tetanus, a potentially life-threatening disease, is currently rare in the developed nations thanks to vaccination programs, but remains endemic in the developing world due to being unvaccinated or inadequately vaccinated (1). The elderly are at higher risk because

they have decreased levels of protective antibodies. Cancer patients are especially vulnerable to this complication not only because they tend to be an aging population undergoing immunosuppressive therapies, but also because of the presence of fungating/necrotic tumor upon diagnosis. In what follows, we report on a lethal tetanus infection after chemotherapy for breast

cancer, and raise the issue of tetanus prevention in advanced breast cancer patients who are vulnerable to lethal tetanus infection.

Case Report

A 67 year-old woman presented with a large painful left-breast tumor with skin ulceration (Fig. 1A) and grade III infiltrating ductal carcinoma, cT-4N2M0, clinical stage IIIB negative for estrogen receptor (ER) and progesterone receptor (PR), positive for HER2/neu (IHC 3+), as confirmed histologically. Twenty days after the first infusion of neoadjuvant chemotherapy with doxorubicin/cyclophosphamide, trismus, drooling, and lumbar muscular spasm were noticed accompanied by progressive dyspnea, dysphasia and intermittent limb muscle fasciculation. Physical examination revealed stable vital signs but stiff neck, spasm of the masseter muscles with hyper-reflexia. A brain MRI revealed no evident leptomeningeal infection or cancerous involvement. Two days later, there was a sudden onset of apnea and cardiac arrest which was restored after brief resuscitation. Anti-tetanus immunoglobulin, anti-tetanus toxoid, and broad-spectrum antibiotic regimen were infused to eradicate the tetanus spores and mixed flora infection within the necrotic breast tumor. Surgical debridement was also performed to the ulcerated and purulent breast tumor (Fig. 2A). Other supportive measures, including muscle relaxants, sedatives, mechanical ventilation, and inotropic agents were provided. Aerobic and anaerobic culture of the wound discharge revealed polymicrobial infection: not only *Clostridium tetani* but *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Enterococcus*. Four weeks later, she was able to be taken off the ventilator. There was no discharge and the fungating wound was healing well (Fig. 1B and Fig. 2B). Five weeks later, weekly trastuzumab and lapatinib were provided for her over-expressed HER2/neu tumor. The patient was discharged uneventfully and surgical mastectomy was performed smoothly 4 months later showing complete remission of pathology. She remains disease-free 2 years after completion postoperative adjuvant trastuzumab and lapatinib.

Discussion

Tetanus is a devastating neurological disease, leading to high mortality and morbidity. Since it is a rare occurrence nowadays with less general awareness, it could become an unexpected lethal complication in advanced breast cancer before cancer therapy (2, 3). Tetanus is clinically characterized by muscle spasms resulting from neurotoxin-producing *Clostridium tetani*. In our case the diagnosis was based on the clinical picture instead of laboratory detection of antibodies or identification of *Clostridium tetani*. The patient had been well until she received one infusion of cytotoxic chemotherapy, when she presented the typical features of tetanus with ensuing respiratory distress and hemodynamic collapse. The necrotic breast tumor may provide an anaerobic environment prone to *Clostridium tetani*. This raises an important issue: videlicet that chemotherapy might disrupt the well-capsulated necrotic tumor and cause a leak of contained bacterial toxin or form a portal of entry for tetanus infection (3). In addition, patients with necrotic or ulcerated malignant tumors seem to be predisposed to clostridial infections, since not only is immunity impaired in the elderly, but tumors can also become a potential point of entry or a bacterial habitat (4, 5). Thus, proper tetanus vaccination before surgical excision, debridement, or cytotoxic chemotherapy seems justified to prevent this catastrophe (6). Five cases including ours have been reported of tetanus infection attributed to a malignant fungating wound in advanced breast cancer (Table 1) (5, 7, 8). They were all distributed in Asia. Two of the five cases succumbed to fatal complications. Our report suggests that fatal tetanus infection may occur in outsize fungating/necrotic tumor. It raises the important issue of active immunization of patients with large/necrotic tumors against tetanus. Physicians should be aware that immunization may be inadequate in certain groups, while larger studies are called for to establish guidelines for revaccinating elderly cancer patients following chemotherapy (9-11).

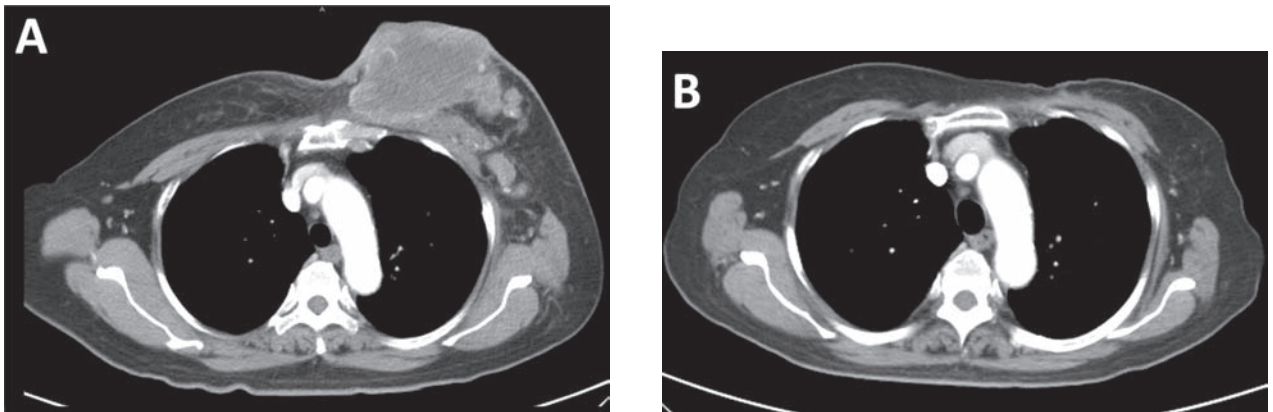


Figure 1. (A) Contrast-enhanced computed tomography of the thorax shows an outside left-breast cancer with major pectoris muscle invasion and multiple nodal metastases. (B) After neoadjuvant chemotherapy, anti-HER2 target therapy, and local surgical debridement, significant disease regression was seen in the left-breast tumor and lymph node metastasis

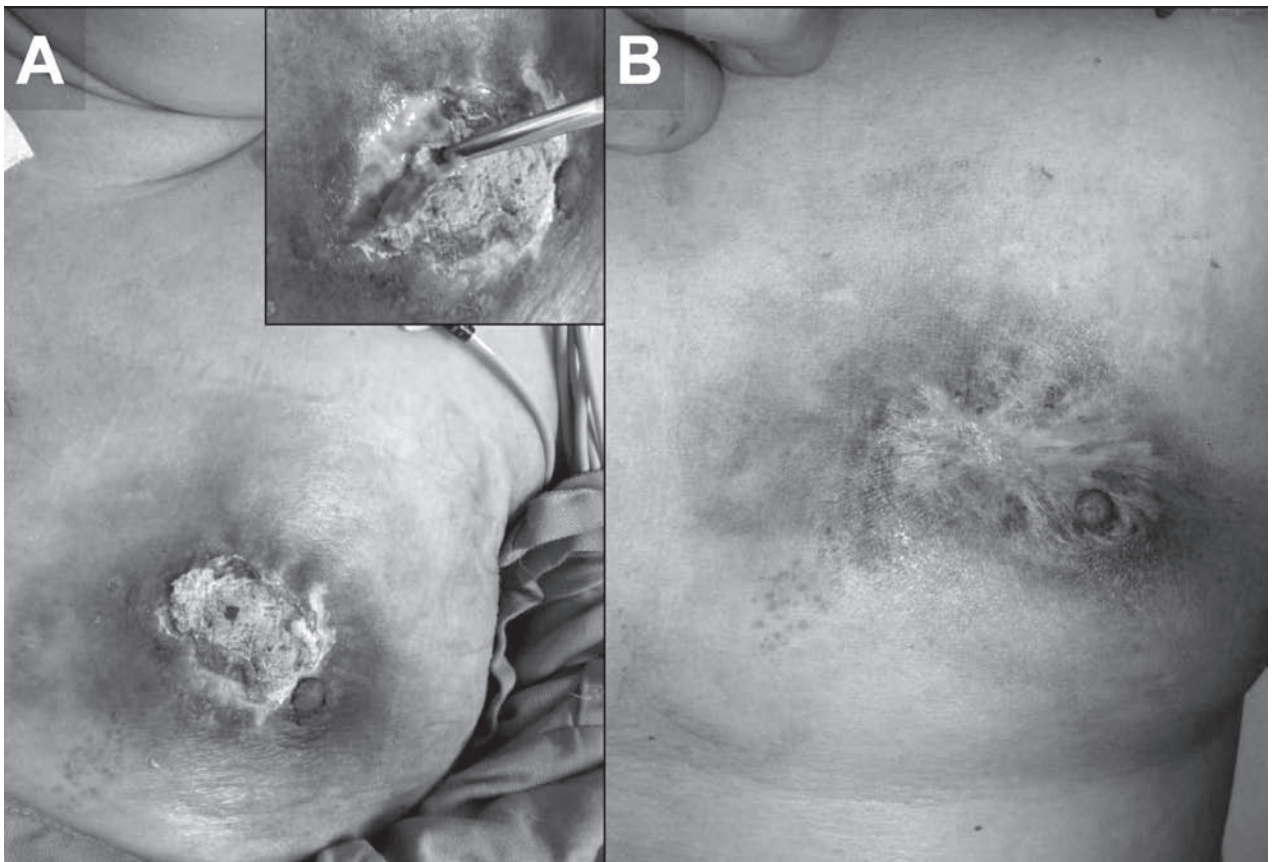


Figure 2. (A) Extensive fungating left-breast tumor with purulent discharge seen in a patient suffering from severe tetanus infection. (B) After surgical debridement and intensive wound care, a healed wound with fibrotic scar formation may be observed, with significant regression of the breast tumor.

Table 1. Clinical characteristics of reported breast cancer patients with tetanus

	1	2	3	4	5
Age	53	59	60	55	67
Nation	Singapore	Malaysia	Sri Lanka	Japan	Taiwan
Staging breast cancer	T4N3cM0, Stage IIIC	T4NxM1, Stage IV	T4NxMx, Stage IIIB	T4N0M0, Phyllodes Tumor	T4N3cM0, Stage IIIC
Initial treatment	None	None	None	None	Chemotherapy
Initial clinical manifestation	Trismus; dysphasia	Trismus, associated with pain	Pain of lower jaw	Trismus; Toothache	Trismus
Wound/tissue culture	<i>Acinetobacter baumannii</i> ; <i>Pseudomonas aeruginosa</i> ; <i>Enterococcus</i>	N/A	N/A	N/A	<i>Clostridium tetani</i> ; <i>Pseudomonas aeruginosa</i> ; <i>Klebsiella pneumoniae</i> ; <i>Enterococcus</i>
Management	Antitetanus Ig; Anti-tetanus toxoid; Penicillin Sedatives; Muscle relaxant; Tracheostomy; wound dressing	Antitetanus Ig; Anti-tetanus toxoid; penicillin Sedatives; Muscle relaxant Tracheostomy; Mastectomy	Mastectomy;	Antitetanus Ig; Anti-tetanus toxoid; Penicillin; Sedatives; Muscle relaxant; Tracheostomy; Mastectomy	Antitetanus Ig; Anti-tetanus toxoid; Penicillin; Sedatives; Muscle relaxant; Tracheostomy; Surgical debridement
Hospital days	39	30	N/A	52	54
Outcome	deceased	recovered	deceased	recovered	recovered
Reference	(7)	(8)	(5)	(3)	Our case

N/A, not available; Ig, immunoglobulin.

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